AMENDMENTS TO THE CLAIMS

1.–25. (Canceled)

26. (Currently amended) A method for ~~determining, in~~ aiding in the determination of whether a mammal~~, the susceptibility~~ is susceptible to or at risk of a disease associated with β-amyloid formation and/or aggregation, ~~for determining, in a mammal, the risk of developing a disease associated with β-amyloid formation and/or aggregation, for screening of the clearance of β-amyloid deposits in a mammal, and/or for predicting the level of β-amyloid burden in a mammal,~~ said method comprising:

(a) determining, in a first sample obtained from said mammal, the total amount of N-terminal truncated and/or post-translationally modified β-amyloid variant;

(b) comparing the amount of β-amyloid variant determined in step (a) with the amount of said ~~N-terminal truncated and/or post-translationally modified β-amyloid~~ variant typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β-amyloid formation and/or aggregation;

(c) concluding, from the comparison in step (b), whether the mammal is susceptible to or at risk of a disease associated with β-amyloid formation and/or aggregation~~, or whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation, whether the β-amyloid deposition in the mammal is cleared, or what the level of β-amyloid burden is in said mammal~~.

27. (Cancelled)

28. (Cancelled)

29. (Currently amended) The method of claim 26 comprising:

(a) determining in the first sample, the amount of one or more N-terminal truncated and/or post-translationally modified β-amyloid variant(s);

(b) comparing the amount determined in step (a) with the amount of the particular N-terminal truncated and/or post-translationally modified β-amyloid variant(s) typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β-amyloid formation and/or aggregation ~~in the second sample~~;

(c) concluding, from the comparison of step (b), whether the mammal is susceptible to or at risk of a disease associated with β-amyloid formation and/or aggregation~~, whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation, whether the β-amyloid deposition in the mammal is cleared, and/or what the level of β-amyloid burden is in the mammal~~.

30. (Currently Amended) The method of claim 29 for aiding in the determination of whether a mammal is susceptible to or at risk of a disease associated with β-amyloid formation and/or aggregation by measuring ~~predicting the~~ said mammal's level of β-amyloid burden ~~in a mammal~~, the method further comprising:

(a) administering to said mammal a composition for eliciting an immune response or ~~a therapeutic composition~~ comprising ~~an~~ one or more particular N-terminal truncated and/or post-translational modified [[A]]β-amyloid variants ~~peptide~~;

(b) determining in a biological fluid sample obtained from said mammal the total amount of N-terminal truncated and/or post-translationally modified β-amyloid variant;

(c) subtracting from the total amount of said β-amyloid variant determined in step (b) the amount of the administered β-amyloid variant(s) present in said biological fluid sample.

(d) comparing the amount of β-amyloid variant determined in step (c) with the amount of ~~said~~ the non-administered ~~N-terminal truncated and/or post-translationally modified β-amyloid~~ variant typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β-amyloid formation and/or aggregation;

(~~d~~e) concluding, from the comparison in step ([c]d) ~~what~~ the level of β-amyloid burden ~~is~~ in said mammal.

31. (Withdrawn) The method of claim 26 wherein said N-terminal truncated β-amyloid variant starts at position 2, 3, 4, 5, 6, 7, 8, 9, or 10 of β-amyloid.

32. (Withdrawn) The method of claim 31 wherein said N-terminal truncated β-amyloid variant starts at position 2, 3, 4, 5, 8, 9, or 10 of β-amyloid.

33. (Withdrawn) The method of claim 32 wherein said N-terminal truncated β-amyloid variant starts at position 3, 4, 5, 8, or 9 of β-amyloid.

34. (Withdrawn) The method of claim 31 wherein said β-amyloid variant is selected from the group consisting of Aβ(2-42), Aβ(3-42), Aβ(4-42), Aβ(5-42), Aβ(6-42), Aβ(7-42), Aβ(8-42), Aβ(9-42) and Aβ(10-42).

35. (Wihdrawn) The method of claim 26 wherein the post-translationally modified β-amyloid variant is modified by methylation or pyroglutamylation.

36. (Withdrawn) The method of claim 35 wherein the methylation is present at position 1, 2, 4, or 6 of an N-terminal truncated β-amyloid variant.

37. (Withdrawn) The method according to claim 35 further characterized in that the pyroglutamylation is present at position 3 of an N-terminal truncated β-amyloid variant starting at position 3 of β-amyloid.

38. (Cancelled)

39. (Currently amended) The method of claim 29~~ 26 for determining in a mammal, the susceptibility to a disease associated with β-amyloid formation and/or aggregation, or for determining, in a mammal, the risk of developing a disease associated with β-amyloid formation and/or aggregation~~ comprising:

(a) determining, in a sample obtained from said mammal[[:]] the amount of antibody or reactive T-cells specific for an N-terminal truncated and/or post-translationally modified [[A]]β-amyloid variant~~ peptide~~;

(b) comparing the amount determined in step (a) with the amount of the antibody or reactive T-cells~~ in a control mammal~~ typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β-amyloid formation and/or aggregation;

(c) concluding, from the comparison in step (b), whether the mammal is susceptible to or at risk for a disease associated with β-amyloid formation and/or aggregation ~~or whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation~~;

wherein an increased amount of antibody or reactive T-cells specific for [[(i)]]N-terminal truncated and/or post-translationally modified [[A]]β-amyloid variant ~~peptide~~ is an indication that the mammal is susceptible to, or at risk of, developing a disease associated with Aβ formation and/or aggregation.

40. (Previously presented) The method of claim 26 wherein at least one of the first and second samples is a brain extract sample or a body fluid sample.

41. (Currently Amended) The method of claim 40 wherein the body fluid sample is a blood sample or a cerebrospinal fluid (CSF) sample.

42. (Previously presented) The method of claim 26 wherein the disease associated with β-amyloid formation and/or aggregation is Alzheimer's disease (AD).

43. (Withdrawn) The method of claim 26 wherein the susceptibility to Alzheimer's disease (AD) or the risk of developing AD is determined by detecting Aβ(5-42) or Aβ(8-42) in a body fluid sample obtained from the mammal.

44.-54. (Cancelled)

55. (New) The method of claim 29 for aiding in the determination of whether a mammal is susceptible to or at risk of a disease associated with β-amyloid formation and/or aggregation by measuring the clearance of β-amyloid deposits in said mammal, the method further comprising:

(a) administering to said mammal a composition for eliciting an immune response or comprising one or more particular N-terminal truncated and/or post-translational modified β-amyloid variants;

(b) determining in a biological fluid sample obtained from said mammal the total amount of N-terminal truncated and/or post-translationally modified β-amyloid variant;

(c) subtracting from the total amount of said β-amyloid variant determined in step (b) the amount of the administered β-amyloid variant(s) present in said biological fluid sample.

(d) comparing the amount of β-amyloid variant determined in step (c) with the amount of the non-administered variants typically present in control samples obtained from one or more patients known to suffer from a particular disease associated with β-amyloid formation and/or aggregation;

(e) concluding, from the comparison in step (d) the amount of β-amyloid cleared.

56. (New) The method of claim 29 wherein said N-terminal truncated β-amyloid variant starts at position 4 of β-amyloid.

57. (New) The method of claim 56 wherein said β-amyloid variant is Aβ(4-42).

58. (New) The method of claim 29 wherein the post-translationally modified β-amyloid variant is modified by methylation.

59. (New) The method of claim 58 wherein the methylation is present at position 4 of an N-terminal truncated β-amyloid variant.

60. (New) The method of claim 29 wherein the susceptibility to Alzheimer's disease (AD) or the risk of developing AD is determined by detecting Aβ(5-42) in a body fluid sample obtained from the mammal.

61. (New) The method of claim 26 wherein the amount of N-terminal truncated and/or post-translationally modified β-amyloid variant is determined by 2-D electrophoresis or mass spectrometry or both.

62. (New) The method of claim 26 wherein the total amount of β-amyloid is detected using an antibody that binds to a β-amyloid epitope towards the C-terminus.

63. (New) The method of claim 29 wherein the amount of one or more N-terminal truncated and/or post-translationally modified β-amyloid variants is detected using an antibody that binds an epitope at the N-terminus of said variants.